

## **REMARKS/ARGUMENTS**

### **Status of the Claims**

Upon entry of the present amendment, claims 1-6, 8-9 and 17-18 are amended. Support for preadipocytes is found throughout the specification, for example, in Example 3 on page 25, line 16 through page 26, line 10 and on page 26, lines 20-28. No new matter is added by the present amendments, and the Examiner is respectfully requested to enter them.

### **Rejoinder of Restricted Species**

The Examiner is thanked for rejoining the species restriction between retroviral and adenoviral vectors.

### **Information Disclosure Statement**

The Examiner is thanked for reviewing and acknowledging documents DP-DT and EA-EK submitted on Forms SB/08.

### **Claim Objections**

The Examiners objection to claims 2-5 has been addressed by amending the claims to recite "The preadipocyte population of . . ." Accordingly, the Examiner is respectfully requested to withdraw this objection.

### **Rejection under 35 U.S.C. § 112, first paragraph, new matter**

The Examiner has rejected claims 1-7, 9-11, 18 and 19 under 35 U.S.C. § 112, first paragraph, as allegedly containing new matter. In particular, the Examiner objects to the phrase "is substantially free of non-adipocyte cells." Applicants do not agree with the Examiner. However, in the interest of furthering prosecution, Applicants have amended claims 1, 6, 9 and 18 to remove the language found objectionable to the Examiner. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

**Rejection under 35 U.S.C. § 102(e)**

The Examiner has rejected claims 1-5, 8-9 and 17 under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent No. 7,015,037 ("Furcht"). Applicants do not agree with the Examiner's position. However, in the interest of furthering prosecution, Applicants have amended the claims to set forth a population of primary cultured preadipocytes that stably maintain a foreign DNA encoding a protein that is secreted outside of a cell, methods of production of such preadipocytes, and implants containing such preadipocytes. Furcht does not disclose or suggest a population of preadipocytes or introducing a foreign gene into a preadipocyte cell. Instead, Furcht discloses differentiated, mature adipocytes derived from multipotent adult stem cells. The Examiner acknowledges that the specification defines preadipocytes as stromal cells that have not yet differentiated. *See*, page 5 of the present Office Action. Therefore, the amended claims are novel over Furcht. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

**Rejections under 35 U.S.C. § 103(a)**

**Furcht in view of Crystal, further in view of Baetge**

Claims 9-11 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Furcht in view of U.S. Patent Publication No. 2002/0076395 ("Crystal"), and further in view of U.S. Patent No. 5,639,275 ("Baetge").

To establish a *prima facie* case of obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference must teach or suggest all the claims limitations. M.P.E.P. § 2143.

Here, the combined disclosures of Furcht, Crystal and Baetge do not disclose or suggest each and every element of the claimed invention. As discussed above, the present claims have been amended so that they are directed to a population of primary cultured "preadipocytes". Furcht fails to teach or suggest primary cultured preadipocytes of any kind, much less preadipocytes that stably maintain a foreign DNA encoding a protein that is secreted outside of a

cell. Crystal and Baetge do not cure the deficiencies of Furcht. Instead, Crystal discloses using mature adipocytes to create implants and Baetge does not disclose or suggest anything about adipocytes at all.

Furthermore, Applicants submit that the population of primary cultured preadipocytes and the implant composition of the present invention comprising a population of primary cultured preadipocytes, possess advantageous effects compared to compositions comprising mature adipocytes. Specifically, the mature adipocytes disclosed by Furcht, which are differentiated from stem cells, and the mature adipocytes comprised in the implant composition of Crystal do not proliferate. In direct contrast, the population of primary cultured preadipocytes, isolated and comprised in the claimed implant does proliferate. This produces practically important advantages, *i.e.*, the population of preadipocytes can be grown to increase the number of cells to be implanted while retaining the homogeneity of the population. The population of preadipocytes can be frozen for preservation and, by using this frozen population, cells prepared in the same production lot can be repeatedly used for implantation.

Because the combined disclosures of Furcht, Crystal and Baetge fail to disclose or suggest all of the elements of the claimed invention, they do not render the present invention obvious. Accordingly, the Examiner is respectfully requested to withdraw the present rejection.

Furcht in view of Hertzl

Claims 6-7 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Furcht in view of Hertzl *et al.*, *J. Lipid Res.* (2000) 41:1082-1086 ("Hertzl"). To the extent that this rejection applies to the amended claims, Applicants respectfully traverse. The combined disclosures of Furcht and Hertzl do not disclose or suggest each and every element of the claimed invention.

Claim 6 is directed to methods of producing populations of primary cultured preadipocytes. As discussed above, Furcht does not disclose or suggest any population of primary cultured preadipocytes or introducing a foreign gene into a preadipocyte. Instead, Furcht discloses mature, differentiated adipocytes derived from multipotent adult stem cells.

Furcht discloses transferring a foreign gene into multipotent adult stem cells. The stem cells taught in Furcht are distinguishable from preadipocytes.

Hertzel does not supply the elements missing from Furcht. The differentiated, primary adipocytes described in Hertzel are also clearly distinguishable from preadipocytes. To prepare primary adipocytes from gonadal fat pads of mice, Hertzel conducted “repeated (three or four) washes with supplemented KRH buffer followed by centrifugation at 4,000 rpm for 10 min” (see “Primary adipocytes” on page 1082). At the end of this washing procedure, they recovered “the *floating adipocytes*,” and thus would not be able to isolate preadipocytes, which are heavier than mature adipocytes and should precipitate when subjected to centrifugation under the conditions described by Hertzel. In fact, Hertzel’s primary adipocytes shown in Figures 1 and 2 are all round-shaped, and none of the cells has fibroblast-like morphology. This indicates that the primary adipocytes disclosed by Hertzel do not include preadipocytes.

Clearly, the claimed methods are different from those described by Furcht and Hertzel in terms of types of cells subjected to gene transduction. Thus, even if one skilled in the art could combine the teachings of Furcht and Hertzel, their combined disclosures still do not disclose or suggest the claimed invention, which uses preadipocytes as a target of gene transduction.

Since the combination of the Furcht and Hertzel fails to teach or suggest all of the elements of the claimed invention, a *prima facie* case of obviousness against claims 6 and 7 has not been established. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

Furcht in view of Hertzel, further in view of Zhang

Claim 6 and 19 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Furcht in view of Hertzel, and further in view of Zhang, *et al.*, *J. Endocrinology* (2000) 164:119-128. For the reasons discussed above, neither Furcht nor Hertzel disclose or suggest any methods of producing populations of primary cultured preadipocytes. Zhang does not supply the elements missing from Furcht and Hertzel. Instead, Zhang discloses using ceiling culture techniques to enrich for mature adipocytes, while minimizing or eliminating contaminating

preadipocytes. *See, e.g.*, Zhang at page 125, right column, bottom paragraph; and page 127, left column, top paragraph. Zhang teaches those of skill how to avoid preadipocyte populations, because Zhang considers them to be a contaminating factor in a population of mature, differentiated adipocytes.

Because the combined disclosures of Furcht, Hertzelt and Zhang fail to disclose or suggest all of the elements of the claimed invention, they do not render the present invention obvious. Accordingly, the Examiner is respectfully requested to withdraw the present rejection.

### CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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